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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/877,220	06/08/2001	Karin Westlund High	265.0019 0101	8535

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EXAMINER	
BRANNOCK, MICHAEL T	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 05/26/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/877,220	HIGH ET AL.	
	Examiner	Art Unit	
	Michael Brannock	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 March 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *30,31,34,35,46,47,54,55 and 68-87* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *30, 31, 34, 35, 46, 47, 54, 55, 68-87* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 April 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application: Claims and Amendments

Applicant is notified that the amendments put forth on 3/23/05, have been entered in full.

Response to Amendment

Applicant is notified that any outstanding objection or rejection that is not expressly maintained in this Office action has been withdrawn in view of Applicant's amendments.

Applicant is notified that the finality of the prior Office action is withdrawn in view of the issues below. In the Interview of 4/22/05, the examiner explained that the prior rejections of claims 29-31 and 60-67 under 35 U.S.C. 112, first paragraph, at pages 6-9 of the Office Action mailed 5/18/04 were erroneously withdrawn in the Final Office Action mailed 12/23/04. The examiner indicated that these rejections would be applicable to amended claims 30 and 31 proposed in Applicant's response (3/23/05). Additionally, the indicated allowability of claims 30, 31, 34, 35, 46, 47, 54 and 55 is withdrawn in view of the issues below.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 30 and 31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of altering the NR1 subunit distribution in a cell, wherein the alteration in the total amount of NR1 subunit in the cell increases or decreases, and the nuclear translocation of NR1 is altered, comprising contacting a cell with a tyrosine kinase

inhibitor or tyrosine phosphatase inhibitor, does not reasonably provide enablement the above such alterations comprising contacting the cell with any other type of compound . The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The specification discloses experiments where in tyrosine kinase inhibitors are used to inhibit the NMDA-receptor-activity dependent translocation of the NR1 subunit to the nucleous; this inhibition is also accompanied by an inhibition of the NMDA-receptor-activity dependent increase in the total amount of NR1 subunit, see Examples I and II. Claim 31 specifically requires the opposite effect, i.e. that the presence of the compound increase the total amount of NR1 in the cell. No such compounds were demonstrated to do this, however, it is generally assumed that effects opposite of tyrosine kinase inhibitors can be achieved using tyrosine phosphatase inhibitors, as exemplified by Wang, YT et al., PNAS 93(1721-1725)1996, see the Abstract.

The instant claims, however, encompass any and all compounds that may one day prove to have this effect, yet are not disclosed in the specification. And one of ordinary skill in the art would not expect that all or most compounds could alter the subcellular distribution of the NR1 subunit, and of those that could, Rao et al,., Neuron, 19(801-812)1997 teach that one could not expect that the total amount of the NR1 subunit or its nuclear translocation would be altered, see the first paragraph of page 803. The instant claims to the use of this large genera is not supported by a commensurate teaching as to which compounds could actually be used. The claims are, in essence, single means claims, because the claims encompass any composition having the recited activities whereas the instant specification only discloses those two types of

compositions known to the inventor, i.e. tyrosine kinsase inhibitors and tyrosine phosphatase inhibitors. In *In re Hyatt*, 708 F.2d 712, 218 USPQ 195 (Fed. Cir. 1983), a single means claim which covered every conceivable means for achieving the stated purpose was held nonenabling for the scope of the claim because the specification at most disclosed only those means known to the inventors. When claims depend on a recited property, a fact situation comparable to *Hyatt* is possible, where the claim covers every conceivable structure (means) for achieving the stated property (result) while the specification discloses at most only those known to the inventor. See also *Fiers v. Sugano*, 984 F.2d 164, 25 USPQ2d 1601 (Fed. Cir. 1993), and MPEP § 2164.08(a).

Thus, the specification has simply offered an invitation to begin a trial and error course of experimentation to try to find other such compounds, if they can be found, to try to find compounds that could be used commensurate with that which is claimed. Such random trial and error experimentation is unduly burdensome. See suggested claim language below.

In Applicant's response of 8/17/04, Applicant argued that tyrosine kinases, etc. are well known in the are well known in the art and therefore the amount of experimentation would not be undue. This argument has been fully considered but not deemed persuasive for the reasons put forth above, also one skilled in the art appreciates that tyrosine kinases etc have substrate specificity and would not be expected to be able to be used as the tyrosine kinase inhibitors were that have a much more generalized activity. Thus the artisan would not know which, if any, of the known tyrosine kinases etc. to use to accomplish the method. An invitation to try and find such does not constitute an enabling disclosure.

Claims 30 and 31 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification discloses that tyrosine kinsase inhibitors and tyrosine phosphatase inhibitors can alter the nuclear localization and total amount of NR1 in a cell yet the claims encompass the use of any compounds, yet to be discovered that could accomplish this. The instant disclosure of compounds having a single mode of action, i.e. modulating tyrosine phosphorylation, does not adequately support the scope of the claimed genus, which encompasses a substantial variety of subgenera. A genus claim may be supported by a representative number of species as set forth in *Regents of the University of California v Eli Lilly & Co,* 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. The instant specification discloses, however, compounds having a single mode of action which is not sufficient to describe the large and disparate genera encompassed by the claims.

With the exception of tyrosine kinsase inhibitors and tyrosine phosphatase inhibitors referred to above, the skilled artisan cannot envision the detailed chemical structure of the encompassed compounds and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and

reference to a potential method of isolating it. The nucleic acid itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only tyrosine kinsase inhibitors and tyrosine phosphatase inhibitors, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115). See suggested claim language below.

In Applicant's response of 8/17/04, Applicant argues that the examiner wrongly alleged that only polynucleotide sequences were disclosed in the instant specification. This argument has been fully considered but not deemed persuasive. The examiner's intention was to draw the analogy between the recited court cases and the instant fact pattern, wherein polynucleotides were considered to be compounds as would be the tyrosine kinases, etc. in the instant fact pattern.

New Rejection:

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 30, 31, 34, 35, 46, 47, 54, 55, 68-87 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for the following reasons.

In claims 30 and 31 the phrase "the control cell not contacted with the compound" lacks antecedent bases in the claim, thus the artisan would not know which control cell not contacted with the compound was *the* control cell not contacted with the compound.

Claims 34, 35, 46, 47, 54, 55 and dependent claims "a cell not contacted" yet the claims do not set forth what cell is "a cell not contacted", e.g. are cells other than "a control cell not contacted with the compound", as in claims 30 and 31, included in the scope of the claim?

Claims 30, 31, 34, 35, 46, 47, 54, 55 and dependent claims are indefinite because they set forth a broad limitation in the preamble yet it is unclear if the claim contains sufficient steps to accomplish the goal set forth in the preamble, i.e. such an omission amounting to a gap between the steps. See MPEP § 2172.01. See suggested claim language below.

Claims 46 and 47 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claims 46 and 47 appear to be of identical scope as claims 34 and 35. Although claims 46 and 47 recite the step of detecting the amount of NR1

subunit in the cell, the claims are further limited such that the alteration is in the amount of NR1 subunit associated with the nucleus; this is identical in scope to that of clams 34 and 35, respectively. See suggested claim language below

Claim Objections

Claim 55 is objected to because of the following informalities: claim 55 requires that the tyrosine kinase inhibitor *increase* the amount of NR1 associated with the nucleus. This appears to be a clerical error as this effect is contrary to the teachings of the specification. Replacing "kinase" with "phosphatase" would obviate this objection. Appropriate correction or clarification is required.

The following claims would be allowable.

30. A method for altering NR1 subunit distribution in a test cell by decreasing the amount of NR1 subunit associated with a nucleus of the test cell, the method comprising:

contacting the test cell with a tyrosine kinase inhibitor,

activating an NMDA glutamate receptor present on the test cell and on a control cell not contacted with the tyrosine kinase inhibitor, and;

detecting the distribution of NR1 subunit associated with the nucleus in the test cell and the control cell, wherein a decrease in the amount of NR1 subunit associated with the nucleus of the test cell relative to the control cell indicates the alteration of NR1 subunit distribution.

31. A method for altering NR1 subunit distribution in a test cell by increasing the amount of NR1 subunit associated with a nucleus of the test cell, the method comprising:

contacting the test cell with a tyrosine phosphatse inhibitor,

activating an NMDA glutamate receptor present on the test cell and on a control cell not contacted with the tyrosine kinase inhibitor, and;

detecting the distribution of NR1 subunit associated with the nucleus in the test cell and the control cell, wherein an increase in the amount of NR1 subunit associated with the nucleus of the test cell relative to the control cell indicates the alteration of NR1 subunit distribution.

34. A method for identifying a compound that alters NR1 subunit distribution in a test cell by decreasing the amount of NR1 subunit associated with a nucleus of the test cell, the method comprising:

contacting the test cell with a compound,

activating an NMDA glutamate receptor present on the test cell and on a control cell not contacted with the compound, and;

detecting an alteration in the distribution of NR1 subunit in the test cell, wherein a decrease in the amount of NR1 subunit associated with a nucleus of the test cell relative to the control cell indicates the compound alters NR1 subunit distribution in the test cell.

35. A method for identifying a compound that alters NR1 subunit distribution in a test cell by increasing the amount of NR1 subunit associated with a nucleus of the test cell, the method comprising:

contacting the test cell with a compound,

activating an NMDA glutamate receptor present on the test cell and on a control cell not contacted with the compound, and;

detecting an alteration in the distribution of NR1 subunit in the test cell, wherein an increase in the amount of NR1 subunit associated with a nucleus of the test cell relative to the control cell indicates the compound alters NR1 subunit distribution in the test cell.

46. A method for identifying a compound that alters NR1 subunit distribution in a test cell by decreasing the amount of NR1 subunit associated with a nucleus of the test cell and decreasing the total amount of NR1 subunit in the cell, the method comprising:

contacting the test cell with a compound,

activating an NMDA glutamate receptor present on the test cell and on a control cell not contacted with the compound, and;

detecting a decrease in the amount of NR1 subunit associated with a nucleus of the test cell relative to the control cell,

detecting a decrease in the total amount NR1 subunit in the test cell relative to the control cell, wherein detecting a decrease in the amount of NR1 subunit associated with the nucleus of the test cell relative to the control cell and a decrease in the total amount of NR1 in the test cell relative to the control cell indicates that the compound alters the amount of NR1 subunit associated with a nucleus of the test cell and the total amount of NR1 in the test cell.

47. A method for identifying a compound that alters NR1 subunit distribution in a test cell by increasing the amount of NR1 subunit associated with a nucleus of the test cell and decreasing the total amount of NR1 subunit in the cell, the method comprising:

contacting the test cell with a compound,

activating an NMDA glutamate receptor present on the test cell and on a control cell not contacted with the compound, and;

detecting an increase in the amount of NR1 subunit associated with a nucleus of the test cell relative to the control cell,

detecting a increase in the total amount NR1 subunit in the test cell relative to the control cell, wherein detecting a increase in the amount of NR1 subunit associated with the nucleus of the test cell relative to the control cell and an increase in the total amount of NR1 in the test cell relative to the control cell indicates that the compound alters the amount of NR1 subunit associated with a nucleus of the test cell and the total amount of NR1 in the test cell.

54. A method for identifying a tyrosine kinase inhibitor that alters NR1 subunit distribution in a test cell by decreasing the amount of NR1 subunit associated with a nucleus of the test cell, the method comprising:

contacting the test cell with the tyrosine kinase inhibitor,

activating an NMDA glutamate receptor present on the test cell and on a control cell not contacted with the tyrosine kinase inhibitor; and;

detecting an alteration in the distribution of NR1 subunit in the test cell, wherein detecting a decrease in the amount of NR1 subunit associated with a nucleus of the test cell relative to the control cell indicates the tyrosine kinase inhibitor alters NR1 subunit distribution in the test cell.

55. A method for identifying a tyrosine phosphatase inhibitor that alters NR1 subunit distribution in a test cell by increasing the amount of NR1 subunit associated with a nucleus of the test cell, the method comprising:

contacting the test cell with the tyrosine phosphatase inhibitor,

activating an NMDA glutamate receptor present on the test cell and on a control cell not contacted with the tyrosine kinase inhibitor; and;

detecting an alteration in the distribution of NR1 subunit in the test cell, wherein detecting an increase in the amount of NR1 subunit associated with a nucleus of the test cell relative to the control cell indicates the tyrosine kinase inhibitor alters NR1 subunit distribution in the test cell.

Conclusion

Please note the new central fax number for official correspondence below:

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Brannock, Ph.D., whose telephone number is (571) 272-0869. The examiner can normally be reached on Mondays through Fridays from 10:00 a.m. to 4:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, Ph.D., can be reached at (571) 272-0829. Official papers filed by fax should be directed to 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

MB

Elizabeth C. Kemmerer

ELIZABETH KEMMERER
PRIMARY EXAMINER

May 23, 2005